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Water treatment equipment for haemodialysis applications and related therapies

Équipement de traitement de l'eau pour des applications en hémodialyse et aux thérapies apparentées

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Foreword

ISO (the International Organization for Standardization) is a worldwide federation of national standards bodies (ISO member bodies). The work of preparing International Standards is normally carried out through ISO technical committees. Each member body interested in a subject for which a technical committee has been established has the right to be represented on that committee. International organizations, governmental and non-governmental, in liaison with ISO, also take part in the work. ISO collaborates closely with the International Electrotechnical Commission (IEC) on all matters of electrotechnical standardization.

International Standards are drafted in accordance with the rules given in the ISO/IEC Directives, Part 2.

The main task of technical committees is to prepare International Standards. Draft International Standards adopted by the technical committees are circulated to the member bodies for voting. Publication as an International Standard requires approval by at least 75 % of the member bodies casting a vote.

Attention is drawn to the possibility that some of the elements of this document may be the subject of patent rights. ISO shall not be held responsible for identifying any or all such patent rights.

ISO 26722 was prepared by Technical Committee ISO/TC 150, *Implants for surgery*, Subcommittee SC 2, *Cardiovascular implants and extracorporeal systems*.

Introduction

This International Standard reflects the conscientious efforts of concerned physicians, clinical engineers, nurses, dialysis technicians and dialysis patients, in consultation with device manufacturers and government representatives, to develop an International Standard for performance levels that could be reasonably achieved at the time of publication. The term “consensus,” as applied to the development of voluntary medical device International Standards, does not imply unanimity of opinion, but rather reflects the compromise necessary in some instances when a variety of interests must be merged.

The provisions of this International Standard apply to individual water treatment devices and to water treatment systems assembled from one or more of these devices. In the first instance, this International Standard is directed at the individual or company that specifies the complete water treatment system and, second, at the supplier who assembles and installs the system. Since systems may be assembled from a number of individual water treatment devices, the provisions of this International Standard are also directed at the manufacturers of these devices, provided that the manufacturer indicates that the device is intended for use in haemodialysis applications. This International Standard is written principally to address water treatment systems for dialysis facilities treating multiple patients. However, many of its provisions equally apply to water treatment systems used in applications where a single patient is treated, such as in a home dialysis or acute hospital dialysis setting. Specifically, requirements for the chemical and microbiological quality of water are considered to apply in all settings, regardless of whether a single patient or many patients are being treated.

The verbal forms used in this International Standard conform to usage described in Annex H of the ISO/IEC Directives, Part 2. For the purposes of this International Standard, the auxiliary verb:

— “shall” means that compliance with a requirement or a test is mandatory for compliance with this International Standard;

— “should” means that compliance with a requirement or a test is recommended but is not mandatory for compliance with this International Standard;

— “may” is used to describe a permissible way to achieve compliance with a requirement or test.

The requirements established by this International Standard will help protect haemodialysis patients from adverse effects arising from known chemical and microbial contaminants found in water supplies. However, proper dialysis and patient safety is ultimately dependent on the quality of the dialysis fluid. Since the manufacturer or supplier of water treatment equipment does not have control over the dialysis fluid, any reference to dialysis fluid in this International Standard is for clarification only and not a requirement of the manufacturer. The responsibility for assuring that the dialysis fluid is not contaminated, mismatched, or otherwise damaging to the patient rests with the clinical professionals caring for the patient under the supervision of the medical director. Recommendations on the preparation and handling of water and dialysis fluid in a dialysis facility are provided in ISO 23500.

Water treatment equipment for haemodialysis applications and related therapies

1 Scope

This International Standard is addressed to the manufacturer and/or supplier of water treatment systems and/or devices used for the express purpose of providing water for haemodialysis or related therapies.

This International Standard covers devices used to treat water intended for use in the delivery of haemodialysis and related therapies. Included in the scope of this International Standard is water used for: (1) the preparation of concentrates from powder or other highly concentrated media at a dialysis facility; (2) the preparation of dialysis fluid that may be used for the preparation of substitution fluid; (3) the reprocessing of dialysers for multiple uses.

Included within the scope of this International Standard are all devices, piping and fittings between the point at which potable water is delivered to the water treatment system and the point of use of the dialysis water. Examples of devices included within the scope of this International Standard are water purification devices, online water quality monitors (such as conductivity monitors), and piping systems for the distribution of dialysis water.

Excluded from the scope of this International Standard are dialysis fluid supply systems that proportion water and concentrates to produce dialysis fluid, sorbent dialysis fluid regeneration systems that regenerate and recirculate small volumes of the dialysis fluid, dialysis concentrates, haemodiafiltration systems, haemofiltration systems, systems that process dialysers for multiple uses, and peritoneal dialysis systems. Some of these devices, such as dialysis fluid delivery systems and concentrates, are addressed in other International Standards. Also excluded from the scope of this International Standard are requirements for the ongoing monitoring of the purity of water used for dialysis fluid, concentrate preparation or dialyser reprocessing.

2 Normative references

The following referenced documents are indispensable for the application of this document. For dated references, only the edition cited applies. For undated references, the latest edition of the referenced document (including any amendments) applies.

ISO 13959:2009, *Water for haemodialysis and related therapies*

3 Terms and definitions

For the purposes of this document, the following terms and definitions apply.

3.1
action level
concentration of a contaminant at which steps should be taken to interrupt the trend toward higher, unacceptable levels

3.2
chlorine, combined
chlorine that is chemically combined, such as in chloramine compounds

NOTE No direct test exists for measuring combined chlorine, but it can be measured indirectly by measuring both total and free chlorine and calculating the difference.

3.3
chlorine, free
dissolved molecular chlorine

3.4
chlorine, total
sum of **combined chlorine** (3.2) and **free chlorine** (3.3)

NOTE Chlorine can exist in water as dissolved molecular chlorine (free chlorine) or in chemically combined forms (combined chlorine). Where chloramine is used to disinfect water supplies, chloramine is usually the principal component of combined chlorine.

3.5
device
individual water purification unit, such as a softener, carbon adsorption bed, reverse osmosis unit or deionizer

NOTE This term is synonymous with the term “component” as used by the U.S. Food and Drug Administration (see Reference [26]).

3.6
dialysis fluid
aqueous fluid containing electrolytes and usually buffer and glucose, which is intended to exchange solutes with blood during haemodialysis

NOTE 1 The word “dialysis fluid” is used throughout this document to mean the fluid made from dialysis water and concentrates which is delivered to the dialyser by the dialysis fluid delivery system. Such phrases as “dialysate,” “dialysis solution,” or “dialysing fluid” may be used in place of dialysis fluid.

NOTE 2 The dialysis fluid entering the dialyser is referred to as “fresh dialysis fluid,” while the fluid leaving the dialyser is referred to as “spent dialysis fluid.”

NOTE 3 Dialysis fluid does not include prepackaged parenteral fluids used in some renal replacement therapies, such as haemodiafiltration and haemofiltration.

3.7
dialysis fluid delivery system
device that: (1) prepares dialysis fluid online from dialysis water and concentrates or that stores and distributes premixed dialysis fluid; (2) circulates the dialysis fluid through the dialyser; (3) monitors the dialysis fluid for temperature, conductivity (or equivalent), pressure, flow and blood leaks; (4) prevents dialysis during disinfection or cleaning modes

NOTE 1 The term includes reservoirs, conduits, proportioning devices for the dialysis fluid, and monitors and associated alarms and controls assembled as a system for the purposes listed above.

NOTE 2 The dialysis fluid supply system can be an integral part of the single patient dialysis machine or a centralized preparation system which feeds multiple bedside monitoring systems.

NOTE 3 Dialysis fluid delivery systems are also known as proportioning systems and dialysis fluid supply systems.

3.8
dialysis water
water that has been treated to meet the requirements of ISO 13959 and which is suitable for use in haemodialysis applications, including the preparation of dialysis fluid, reprocessing of dialysers, preparation of concentrates and preparation of substitution fluid for online convective therapies

3.9
disinfection
destruction of pathogenic and other kinds of microorganisms by thermal or chemical means

NOTE 1 Disinfection is a less lethal process than sterilization, because it destroys most recognized pathogenic microorganisms but does not necessarily destroy all microbial forms.

NOTE 2 This definition of "disinfection" is equivalent to low-level disinfection in the Spaulding classification.

3.10
empty bed contact time
EBCT
time taken by a fluid to pass through an empty volume equal to the volume of a particle bed

NOTE 1 EBCT (min) is calculated using the following equation:

$$\text{EBCT} = V/Q$$

where

V is the volume of the particle bed in cubic metres;

Q is the flowrate of water through the bed in cubic metres per minute.

NOTE 2 EBCT is used as an indirect measure of how much contact occurs between particles, such as activated carbon, and water as the water flows through a bed of particles.

3.11
endotoxin
major component of the outer cell wall of gram-negative bacteria

NOTE Endotoxins are lipopolysaccharides, which consist of a polysaccharide chain covalently bound to lipid A. Endotoxins can acutely activate both humoral and cellular host defences, leading to a syndrome characterized by fever, shaking, chills, hypotension, multiple organ failure and even death if allowed to enter the circulation in a sufficient dose.

3.12
feed water
water supplied to a water treatment system or an individual component of a water treatment system

3.13
germicide
agent that kills microorganisms

3.14
haemodiafiltration
form of renal replacement therapy in which waste solutes are removed from blood by a combination of diffusion and convection through a high-flux membrane

NOTE Diffusive solute removal is achieved using a dialysis fluid stream as in haemodialysis. Convective solute removal is achieved by adding ultrafiltration in excess of that needed to obtain the desired weight loss; fluid balance is maintained by infusing replacement solution into the blood either before (pre-dilution haemodiafiltration) or after the dialyser (post-dilution haemodiafiltration).

3.15
haemodialysis
form of renal replacement therapy in which waste solutes are removed primarily by diffusion from blood flowing on one side of a membrane into dialysis fluid flowing on the other side

NOTE Fluid removal that is sufficient to obtain desired weight loss is achieved by establishing a hydrostatic pressure gradient across the membrane. This fluid removal provides some additional waste solute removal, particularly for higher molecular weight solutes.

3.16
haemofiltration
form of renal replacement therapy in which waste solutes are removed from blood by convection

NOTE 1 Convective transport is achieved by ultrafiltration through a high-flux membrane. Fluid balance is maintained by infusing a replacement solution into the blood either before the haemofilter (pre-dilution haemofiltration) or after the haemofilter (post-dilution haemofiltration).

NOTE 2 There is no dialysis fluid stream in haemofiltration.

3.17
manufacturer
person who designs, manufactures, fabricates, assembles, formulates or processes a finished device

NOTE Manufacturers include, but are not limited to, those who perform the functions of contract sterilization, installation, relabelling, remanufacturing, repacking or specification development, and initial distributors of foreign entities performing these functions. The term does not cover preparation of concentrates from prepackaged dry chemicals at a dialysis facility or the handling of bulk concentrates at a dialysis facility after responsibility for the concentrate is transferred from the manufacturer to the user.

3.18
microbial
referring to microscopic organisms, bacteria, fungi and so forth

3.19
microfilter
filter designed to remove particles larger than 0,1 µm in size

NOTE Microfilters have an absolute size cut-off and are available in both dead-end and cross-flow configurations. Some microfilters remove endotoxin by a process of adsorption and endotoxin aggregates greater than 0,1 µm in size may be removed by size exclusion.

3.20
product water
water produced by a water treatment system or individual device thereof

3.21
source water
water entering a dialysis facility from an external supplier, such as a municipal water supply

NOTE Source water is assumed to be potable water.

3.22
total dissolved solids
TDS
sum of all ions in a solution, often approximated by means of electrical conductivity or resistivity measurements

NOTE TDS measurements are commonly used to assess the performance of reverse osmosis units. TDS values are often expressed in terms of $CaCO_3$, NaCl, KCl or 442 equivalents (mg/l). [442 is a solution of sodium sulfate (40 %), sodium bicarbonate (40 %) and sodium chloride (20 %) that closely represents the conductivity to concentration relationship, on average, for naturally occurring fresh water.]

3.23
user
physician or physician's representative responsible for the actual production and handling of dialysis fluid

NOTE This medical device International Standard is mainly directed to device manufacturers, and in that context the “user” is as noted above.

3.24
water treatment system
collection of water purification devices and associated piping, pumps, valves, gauges, etc., that together produce dialysis water meeting the requirements of ISO 13959 for haemodialysis applications and deliver it to the point of use

NOTE See also **device** (3.5).

4 Requirements

4.1 Dialysis water quality requirements

4.1.1 General

The requirements contained in this International Standard apply to the dialysis water as it enters the equipment used to prepare concentrates from powder or other concentrated media at a dialysis facility, to prepare dialysis fluid, or to reprocess dialysers for multiple uses. As such, these requirements apply to the water treatment system as a whole and not to each of the individual devices that make up the system. However, collectively the individual devices shall produce dialysis water that, at a minimum, meets the requirements of the clause.

4.1.2 Microbiology of dialysis water

Dialysis water used to prepare dialysis fluid or concentrates from powder at a dialysis facility, or to reprocess dialysers for multiple uses, shall contain a total viable microbial count and endotoxin levels as specified in ISO 13959.

The manufacturer or supplier of a complete water treatment and distribution system shall demonstrate that the complete water treatment, storage and distribution system meets the requirements of this International Standard, including those related to action levels, at the time of installation.

NOTE 1 If the manufacturer or supplier does not install the water storage and distribution system, then the responsibility of the manufacturer or supplier is limited to demonstrating that the water treatment system, excluding the water storage and distribution system, meets the requirements of this International Standard. If individual devices of the water treatment system are provided by different manufacturers or suppliers, the person or organization specifying the devices is responsible for demonstrating that the complete system meets the requirements of this International Standard at the time of installation.

For disposable water treatment systems validated by the manufacturer to produce dialysis water meeting the quality requirements of this International Standard for a specified time, monitoring of the incoming feed water is required to assure that the input to the treatment system is in the range for which the system has been validated. The manufacturer's recommendations for monitoring the final dialysis water may be followed when the system is operated according to the manufacturer's instructions. Alternatively, the quality of the dialysis water may be monitored as outlined for non-validated systems.

NOTE 2 Following installation of a water treatment, storage and distribution system, the user is responsible for continued monitoring of the water bacteriology of the system and for complying with the requirements of this International Standard, including those requirements related to action levels.

4.1.3 Maximum level of chemical contaminants

Dialysis water used to prepare dialysis fluid or concentrates from powder at a dialysis facility, or to reprocess dialysers for multiple uses, shall not contain chemical contaminants at concentrations in excess of those in Tables 1 and 2 of ISO 13959 (reproduced as Tables B.1 and B.2). The manufacturer or supplier of a complete water treatment system shall recommend a system capable of meeting the requirements of this clause based on the analysis of the feed water. The system design should reflect possible seasonal variations in feed water quality. The manufacturer or supplier of a complete water treatment and distribution system shall demonstrate that the complete water treatment, storage and distribution system is capable of meeting the requirements of this International Standard at the time of installation.

NOTE 1 If the manufacturer or supplier does not install the water storage and distribution system, then the responsibility of the manufacturer or supplier is limited to demonstrating that the water treatment system, excluding the water storage and distribution system, meets the requirements of this International Standard. If individual devices of the water treatment system are provided by different manufacturers or suppliers, the person or organization specifying the devices is responsible for demonstrating that the complete system meets the requirements of this International Standard at the time of installation.

For disposable water treatment and distribution systems that have been validated to produce dialysis water meeting the quality requirements of this International Standard for a specified time, monitoring of the incoming potable water is required to assure that the input to the treatment system is in the range for which the system has been validated. The manufacturer's recommendation for monitoring the final dialysis water may be followed when the system is operated according to the manufacturer's instructions. Alternatively, the quality of the dialysis water may be monitored as outlined for non-validated systems.

NOTE 2 Following installation of a water treatment, storage and distribution system, the user is responsible for continued monitoring of the levels of chemical contaminants in the water and for complying with the requirements of this International Standard.

4.2 Water treatment equipment requirements

4.2.1 General

4.2.1.1 Water treatment system

The supplier of the feed water or the supplier of the water treatment system or a laboratory specified by the user shall perform chemical analyses on feed water to determine the compatibility of the system with the feed water and the suitability of the system for providing dialysis water meeting the requirements of 4.1.3. The result of the chemical analyses shall be available to the user in charge of dialysis. In the case of an individual device, the person incorporating the device into the water treatment system is responsible for ensuring that incorporation of the device does not compromise the ability of the overall system to deliver dialysis water capable of meeting the requirements of 4.1.2 and 4.1.3.

The water treatment and distribution system should include appropriate pressure gauges, flow meters, sample ports, and other ancillary equipment necessary to allow monitoring of the performance of individual system devices and the system as a whole.

Valves may be included in the water treatment system to allow individual devices to be bypassed when there is device failure or to facilitate replacement of a device. If it is possible to bypass a device of the water treatment system, then the manufacturer or installer of that component shall inform the user of the risks associated with bypassing that device and the need for clearly defining the responsibility for operating the bypass. Where such valves are installed, however, a means should be included to minimize the likelihood that the device will be inadvertently bypassed during normal operation of the system.

Operating controls shall be positioned so as to minimize inadvertent resetting.

Electrical circuits shall be separate from hydraulic circuits and adequately protected from fluid leaks.

4.2.1.2 Materials compatibility

Materials that contact dialysis water (including materials used in piping, storage, and distribution systems) shall not interact chemically or physically with that water so as to adversely affect its purity or quality. Water-contacting surfaces shall be fabricated from non-reactive materials (e.g. plastics) or appropriate stainless steel. The use of materials that are known to cause toxicity in haemodialysis, such as copper, brass, galvanized material or aluminium, is specifically prohibited at any point beyond the water treatment device used to remove contaminating metal ions, most commonly a reverse osmosis system or a deionizer. The materials of any water treatment devices (including piping, storage and distribution systems) shall be compatible with the means used to disinfect those devices. Chemicals infused into the water in the pre-treatment section, such as, chlorine, acid, flocculants and complexing agents, shall be adequately removed from dialysis water before they reach any point of use. Monitors or specific test procedures to verify removal of additives shall be provided.

4.2.1.3 Regenerated or reconstituted devices

All devices that are regenerated or reconstituted at a site remote from the dialysis facility, such as deionizers, shall be disinfected at the time of regeneration or reconstitution so that contaminated water is not reintroduced into the system after regeneration or reconstitution. Separate processes shall be used to ensure no intermixing of devices or their component parts between devices returned from medical or potable water users and devices returned from non-potable water users.

4.2.1.4 Disinfection protection

When the manufacturer recommends chemical disinfectants [see 6.3 y)], means shall be provided to restore the equipment and the system in which it is installed, to a safe condition relative to residual disinfectant prior to the dialysis water being used for dialysis applications. When recommending chemical disinfectants, the manufacturer shall also recommend methods for testing for residual levels of the disinfectants. When disinfection is accomplished automatically by chemical disinfectant, including ozone, or by high temperature procedures, activation of the disinfection system shall result in activation of a warning system and measures to prevent patient exposure to an unsafe condition.

4.2.2 Backflow prevention device

All water treatment systems should be preceded by a backflow prevention device to isolate the system from the potable water supply according to local plumbing codes.

4.2.3 Tempering valves

Tempering valves, if used, shall be sized to accommodate the anticipated range of flow rates of hot and cold water. They shall be fitted with a mechanism to prevent backflow of water into the hot and cold water lines and with a means to monitor the outlet water temperature.

4.2.4 Sediment filters

Sediment filters should have an opaque housing or other means to inhibit proliferation of algae. Filters should be fitted with pressure gauges on the inlet and outlet water lines to monitor the pressure drop, ΔP, across the filter.

NOTE Sediment filters are also known as multimedia or sand filters.

4.2.5 Cartridge filters

Cartridge filters should have an opaque housing or other means to inhibit proliferation of algae. Filters should be fitted with pressure gauges on the inlet and outlet water lines to monitor the pressure drop, ΔP, across the filter.

4.2.6 Softeners

Water softeners should be fitted with a mechanism to prevent water containing the high concentrations of sodium chloride used during regeneration, from entering the product water line during regeneration. Automatic regeneration may be performed on a volume schedule or on a time schedule. For softeners that are regenerated automatically on a time schedule, the face of the timers used to control the regeneration cycle should be visible to the user. Operating controls shall be positioned so as to minimize inadvertent resetting.

4.2.7 Anion exchange resin tank

Anion exchange resin, sometimes referred to as an organic scavenger, can remove organic matter and other contaminants from the source water and protect carbon adsorption media from fouling, which can shorten its effective life for chlorine/chloramine removal. If an organic scavenger is installed to protect the carbon media, the scavenger should be installed upstream of the carbon beds. Anion exchange resins may also be used to remove contaminants that might otherwise foul the reverse osmosis membrane.

4.2.8 Carbon adsorption media

Carbon adsorption is used to remove small organic compounds, chlorine and chloramine. When carbon adsorption is used for the removal of chloramines, it shall be adapted specifically to the maximum anticipated water flow rate of the system and the level of chloramines in the feed water.

Where chloramines are used to disinfect the potable water supply at a level of 1 mg/l or more, two carbon adsorption beds shall be installed in series. Each of the carbon beds shall have an EBCT of at least 5 min at the maximum product water flowrate (a total EBCT of at least 10 min). To avoid overly large beds, carbon beds are sometimes arranged as parallel sets, each set consisting of two beds in series. The beds are equally sized and water flows in parallel through each set. In this situation, each bed shall have a minimum EBCT of 5 min at the maximum flow rate through the bed. When parallel sets of beds are used, the piping should be designed to minimize differences in the resistance to flow from inlet and outlet between each parallel set of beds in order to ensure that water flows equally through all beds. A means shall be provided to sample the product water from the first bed in each series-connected pair and a sample port should be installed following the carbon beds for use in the event of total chlorine breaking through the first bed in a series-connected pair.

NOTE Carbon adsorption systems used to prepare water for portable dialysis systems are exempt from the requirement for the second carbon and a 10 min EBCT, provided there is a redundant means of chloramine removal and that a total chlorine concentration of less than 0,1 mg/l is verified in a sample collected after the primary device before each treatment.

In situations where chloramines are not used to disinfect the water, and the ammonium level in the water is low, one carbon adsorption bed or a carbon cartridge filter with a shorter EBCT might be sufficient.

Exhausted carbon adsorption media shall be discarded and replaced with new media according to a replacement schedule determined by regular monitoring. For example, with two beds, when testing between the beds shows that the first bed is exhausted, the second bed should be moved into the first position, the second bed replaced with a new bed, and the exhausted bed discarded.

Granular activated carbon with an iodine number greater than 900 is considered optimal for chlorine/chloramine removal. However, some source waters, such as those with a high organic content could require alternate types of carbon that are more resistant to organic fouling. These types of carbon may have iodine numbers less than 900. When other forms of carbon or granular activated carbon with an iodine number of less than 900 are used, the manufacturer shall provide performance data to demonstrate that each adsorption bed has the capacity to reduce the total chlorine concentration in the feed water to less than 0,1 mg/l when operating at the maximum anticipated flowrate for the maximum time interval between scheduled testing of the product water for total chlorine. Regenerated carbon shall not be used.

Automatically backwashed carbon beds should be fitted with a mechanism to prevent water containing chlorine or chloramines from entering the feed water line of downstream purification devices, such as reverse osmosis, while the carbon beds are being backwashed. For carbon beds that are backwashed automatically on a time schedule, the face of the timers used to control the backwash cycle should be visible to the user and the timer should be set so that backwashing occurs when dialysis is not being performed.

4.2.9 Chemical injection systems

Sodium bisulphite injected into the source water can be an effective means of reducing chlorine and chloramine concentrations. Ascorbic acid has also been used for this purpose. In addition, reducing the pH of alkaline feed water by the injection of mineral acids can enhance the efficiency of granular activated carbon. Chemical injection systems shall include a means of regulating the metering pump to control the addition of chemical. This control system shall be designed to tightly control the addition of chemical. The control system shall ensure that chemical is added only when water is flowing through the pre-treatment cascade and that it is added in fixed proportion to the water flow or based on some continuously monitored parameter, such as pH, using an automated control system. If an automated control system is used to inject the chemical, there shall be an independent monitor of the controlling parameter. Monitors shall be designed so that the monitor cannot be disabled while a patient is at risk, except for brief, necessary periods of manual control with the operator in constant attention.

4.2.10 Reverse osmosis

When used to prepare water for haemodialysis applications, either alone or as the last stage in a purification cascade, reverse osmosis systems shall be shown to be capable, at installation, of meeting the requirements of 4.1, when tested with the typical feed water of the user, in accordance with the methods described in 5.1.

Reverse osmosis devices shall be equipped with online monitors that allow determination of product water conductivity and should be equipped with monitors that determine rejection rate based on conductivity. Monitors that display resistivity or total dissolved solids (TDS) could be used in place of conductivity monitors. Resistivity, conductivity or TDS monitors shall be temperature-compensated, generally to 25 °C. Monitors shall be designed so that the monitor cannot be disabled while a patient is at risk, except for brief, necessary periods of manual control with the operator in constant attention.

When a reverse osmosis system is the last chemical purification process in the water treatment system, it should include a means of preventing patient exposure to unsafe product water, such as diversion of the product water to drain, in the event of a product water conductivity or rejection alarm. If the reverse osmosis system does not have a means of preventing unsafe product water from entering the dialysis machines, the product water conductivity monitor shall activate audible and/or visual alarms when the product water conductivity exceeds the preset alarm limit. The alarms shall be situated so that they ensure a prompt response by personnel in the patient care area. When an audible alarm is used, the sound emitted by the audible alarm shall be at least 65 decibels (“A” scale) at 3 m and it shall not be possible to silence the alarm for more than 180 s.

4.2.11 Deionization

Deionization systems, when used to prepare water for haemodialysis applications, shall be monitored continuously with monitors generally temperature-compensated to 25 °C, to produce water of 1 MΩ·cm or greater specific resistivity (or conductivity of 1 mS/cm or less). Monitors shall be designed so that the monitor cannot be disabled while a patient is at risk, except for brief, necessary periods of manual control with the operator in constant attention. An audible and visual alarm shall be activated when the product water resistivity falls below 1 MΩ·cm and the product water stream shall be prevented from reaching any point of use, for example by being diverted to a drain. The sound emitted by the audible alarm shall be at least 65 decibels (“A” scale) at 3 m and shall be audible in the patient care area. It shall not be possible to silence these alarms for more than 180 s. Feed water for deionization systems shall be pretreated with activated carbon adsorption, or a comparable alternative, to prevent nitrosamine formation. If a deionization system is the last process in a water treatment system, it shall be followed by an endotoxin-retentive filter or other bacteria- and endotoxin-reducing device.

NOTE The requirements given above for deionization might not apply to electrodeionization (EDI) technology, which can be used as an alternative to deionization following reverse osmosis in haemodialysis applications.

4.2.12 Endotoxin-retentive filters

When an endotoxin-retentive filter is used in a water treatment system for haemodialysis applications, the manufacturer of the filter shall disclose the performance of the filter and the conditions under which that performance can be obtained. It is recommended that filters be configured in a cross-flow mode. However, dead-end filters that have validated endotoxin and bacterial removal characteristics may also be used.

Endotoxin-retentive filters should have an opaque housing or other means to inhibit proliferation of algae. Endotoxin-retentive filters should be fitted with a means of assessing filter integrity and fouling. One suitable means is to monitor the pressure drop, ΔP, across the filter using pressure gauges on the inlet and outlet water lines.

4.2.13 Storage and distribution of dialysis water

4.2.13.1 Piping systems

The dialysis water distribution system shall not contribute chemicals (such as aluminium, copper, lead and zinc) or bacterial contamination to the product water. Dialysis water distribution systems should be designed to minimize bacterial proliferation and biofilm formation, such as by using a continuous recirculation loop with flow in the return line. Areas of stagnant flow (dead zones) in the loop system shall be avoided. Direct feed systems shall include a means of verifiably preventing retrograde flow of water into the distribution loop from the feed side of the reverse osmosis unit.

4.2.13.2 Storage tanks

When used, storage tanks should have a conical or bowl-shaped base and should drain from the lowest point of the base. Bladder tanks and pressurized surge tanks should not be used in the dialysis water distribution system. Storage tanks should have a tight-fitting lid and be vented through a hydrophobic 0,45 µm air filter. Sight tubes should be avoided due to the possible growth of algae and fungi. If an overflow pipe is used it shall be fitted with a means of preventing contamination. Means shall be provided to effectively disinfect any storage tank installed in a dialysis water distribution system. An endotoxin-retentive filter, or some other form of microbial control device, should be installed distal to the storage tank.

4.2.13.3 Ultraviolet irradiators

When used to control bacterial proliferation in dialysis water storage and distribution systems, UV irradiation devices shall emit light at a wavelength of 254 nm and provide a dose of radiant energy of 30 mW·sec/cm^2. If the irradiator includes a calibrated ultraviolet intensity meter, the minimum dose of radiant energy should be at least 16 mW·sec/cm^2. The device shall be sized for the maximum anticipated flow rate according to the manufacturer's instructions. UV irradiators should be followed by an endotoxin-retentive filter.

Ultraviolet irradiation can also be used to control bacteria in the pretreatment section of a water treatment system, such as following carbon adsorption beds to reduce the bacterial burden presented to a reverse osmosis unit.

To prevent the use of sublethal doses of radiation that could lead to the development of resistant strains of bacteria, UV irradiators shall be equipped with a calibrated ultraviolet intensity meter, as described above, or with an online monitor of radiant energy output that activates a visible alarm, which indicates that the irradiation source should be replaced. Alternatively, the irradiation source should be replaced on a predetermined schedule according to the manufacturer's instructions to maintain the recommended radiant energy output.

When ultraviolet irradiators are dipped in a storage tank, to control bacteria, they should be designed to keep the required energy at the farthest position in the tank considering the flow situation during operation. The required energy depends on whether sterilization or bacteriostasis is aimed for.

NOTE The recommendations provided in this clause concern UV irradiators used specifically for bacterial control. UV irradiators also can be used for other applications in a water treatment and distribution system. If an ultraviolet irradiator is utilized for reduction of chlorine or chloramines as an adjunct to carbon adsorption media, the manufacturer should verify the performance of the device and supply instructions regarding minimum radiant energy and wavelength for continuing performance.

4.2.13.4 Hot water sanitation systems

When used to control bacterial proliferation in water treatment, storage and distribution systems, the water heater of a hot water sanitation system shall be capable of delivering hot water at the temperature and for the exposure time specified by the manufacturer. Hot water sanitation systems should be equipped with a monitoring system that indicates if the temperature at the most distal point of the device being sanitized drops below the manufacturer's recommended minimum temperature during the disinfection cycle. When sanitation is accomplished automatically by high temperature procedures, activation of the sanitation system shall result in activation of a system indicating that sanitation is in process. Operating controls should be positioned so as to minimize inadvertent resetting.

NOTE For dialysis water distribution loops, the most distal point is where the water re-enters the storage tank (indirect feed systems) or where the water returns to the reverse osmosis system (direct feed systems).

4.2.13.5 Ozone sanitation systems

When used to control bacterial proliferation in dialysis water storage and distribution systems, an ozone generator shall be capable of delivering ozone at the concentration and for the exposure time specified by the manufacturer. An ozone concentration of 0,2 mg/l to 0,5 mg/l, combined with a contact time of 10 min, measured at the end of the distribution loop, is capable of killing bacteria, bacterial spores and viruses in water. Following sanitation, the residual ozone level should be reduced to less than 0,1 mg/l.

When ozone sanitation systems are used, monitoring of the ambient air ozone levels in the area of the ozone generator shall be performed to ensure compliance with exposure limits established by the appropriate health and safety organization.

Activation of an ozone sanitation system shall result in activation of a system to indicate that sanitation is in process and activation of measures to prevent patient exposure to an unsafe condition. Operating controls shall be positioned so as to minimize inadvertent resetting.

5 Tests

5.1 Compliance with dialysis water quality requirements

5.1.1 General

This clause defines test methods by which compliance with the requirements of Clause 4 can be verified. The subclause numbers below correspond to the subclause numbers of Clause 4 (e.g. 5.1.2 ≡ 4.1.2).

NOTE The test methods listed do not represent the only acceptable test methods available but are intended to provide examples of acceptable methods. Other test methods may be used where comparable sensitivity and specificity can be demonstrated.

The requirements of ISO 13959 apply to the dialysis water as it enters the equipment used to prepare concentrates from powder at a dialysis facility, to prepare dialysis fluid or to reprocess dialysers. As such, these requirements apply to the water treatment system as a whole and not to each of the individual devices that make up the system. However, collectively, the individual devices shall produce water that meets the requirements of ISO 13959 when provided with potable water as received at the facility or dialysis clinic. Tests for compliance with water quality requirements should be performed when the system is operating under stable conditions representing normal operation.

5.1.2 Microbiology of dialysis water

Samples shall be collected immediately prior to where the water re-enters the storage tank in an indirect feed system or immediately prior to where the water returns to the reverse osmosis system in a direct feed system. Additional samples shall be collected at, or immediately prior to, the point where water enters the equipment used to prepare concentrates or reprocess dialysers if the line supplying that equipment with water is separate from the distribution loop supplying the dialysis machines. Samples that cannot be assayed within 4 h can be refrigerated up to 24 h. Total viable counts (standard plate counts) shall be obtained using the membrane filter technique, spread plates or pour plates. The calibrated loop technique shall not be used. Culture media should be tryptone glucose extract agar (TGEA), Reasoners 2A (R2A), or equivalent. Blood agar and chocolate agar shall not be used. Incubation is at 17 °C to 23 °C and colonies shall be counted after 168 h (7 d) of incubation. Alternative incubation conditions and colony counting times may be used if validated and proven to be equivalent or better than the stated conditions. Endotoxin concentrations shall be determined by the LAL assay or kinetic method validated to yield results that are equivalent to LAL.

5.1.3 Maximum level of chemical contaminants

Chemical analyses of the water contaminants listed in ISO 13959, Table 1 (reproduced as Table 1 in Annex B of this document) can be obtained by using methods referenced by the American Public Health Association [3], methods referenced by the U.S. Environmental Protection Agency [24], methods referenced in applicable pharmacopoeia, or other equivalent validated analytical methods.

Compliance with the requirements listed in ISO 13959, Table 2 (reproduced as Table B.2) can be shown in one of three ways.

— Where such testing is available, the individual contaminants in Table 2 can be determined using chemical analysis methods referenced by the American Public Health Association [3], methods referenced by the U.S. Environmental Protection Agency[24], methods referenced in applicable pharmacopoeia, or other equivalent validated analytical methods.

— Where testing for the individual trace elements listed in Table 2 is not available, and the source water can be demonstrated to meet the standards for potable water as defined by the WHO [28] or local regulations, an analysis for total heavy metals can be used with a maximum allowable level of 0,1 mg/l.

— If neither of these options is available, compliance with the requirements of Table 2 can be met by using water that can be demonstrated to meet the potable water requirements of the WHO [28] or local regulations and a reverse osmosis system with a rejection of > 90 % based on conductivity, resistivity or TDS.

Samples shall be collected at the end of the water treatment cascade or at the most distal point in each water distribution loop.

5.2 Compliance with water treatment equipment requirements

5.2.1 General

5.2.1.1 Water treatment system

The need for tests to determine the quality of water used to feed water treatment equipment is dependent upon specific features of the devices. Suppliers of water treatment devices should select and perform such tests (e.g. iron, pH, silica, total dissolved solids, alkalinity and total hardness) as are necessary to ensure the reliable performance of their devices.

5.2.1.2 Materials compatibility

The biocompatibility of materials used in the water treatment system which contact dialysis water can be verified using the tests described in the appropriate *pharmacopeia*, such as leach testing with chemical analysis of the extractables.

5.2.1.3 Regenerated or reconstituted devices

The adequacy of disinfection procedures can be demonstrated by culturing a sample of the device's product water following the disinfection procedure. Where regenerated or reconstituted devices are provided by a vendor as medical devices, the disinfection and intermixing requirements of 4.2.1.3 may be demonstrated by certification that the device has been disinfected using validated procedures during regeneration or reconstitution and that validated procedures have been used to ensure that the devices and their component parts have been kept separate from devices and component parts used in non-potable water applications.

5.2.1.4 Disinfection protection

Compliance with the requirements of 4.2.1.4 for chemical disinfection procedures can be determined by testing for the disinfectant in the product water at the end of the disinfection procedure. If a commercially available chemical disinfectant, such as peracetic acid, is used, an established test for residual disinfectant shall be used according to the test manufacturer's instructions, and the residual level shall be less than that recommended by the manufacturer of the specific disinfectant.

When formaldehyde is used, residual levels can be determined by the Hantzsch reaction, Schiff's reagent or an equivalent test and shall be less than 3 mg/l.

When bleach is used, the residual level shall be less than 0,1 mg/l.

Compliance with the requirements of 4.2.1.4 for high-temperature disinfection can be shown by demonstrating that the product water has returned to a safe temperature.

Compliance with the requirements of 4.2.1.4 for ozone disinfection can be shown by demonstrating that the ozone concentration in the product water has returned to a safe level (less than 0,1 mg/l).

Compliance with the patient protection requirements of 4.2.1.4 can be demonstrated by inspection.

5.2.2 Backflow prevention devices

Compliance with the requirements of 4.2.2 can be determined by visual inspection.

5.2.3 Tempering valves

Compliance with the requirements of 4.2.3 can be determined by visual inspection and review of manufacturer's specifications.

5.2.4 Sediment filters

Compliance with the requirements of 4.2.4 can be determined by visual inspection.

5.2.5 Cartridge filters

Compliance with the requirements of 4.2.5 can be determined by visual inspection.

5.2.6 Softeners

Compliance with the requirements of 4.2.6 can be determined by inspection.

5.2.7 Anion exchange resin tanks

The performance of anion exchange resin tanks can be checked by periodically testing the feed and product water for TOC or tannins. Proper regeneration of the resin tank can be determined by monitoring salt usage and regeneration timer settings.

5.2.8 Carbon adsorption media

Total chlorine removal can be used as an indication of carbon adsorption capacity. A DPD test kit selected for this purpose or a similar method shall be used to detect breakthrough of total chlorine, carbon exhaustion or both. DPD materials shall be those designed for total chlorine detection and shall be used according to manufacturers' instructions. Alternatively, online monitors or “dip and read” test strips based on Michler's thioketone (MTK) may be used to measure the concentration of total chlorine. Tests for both free and total chlorine may also be performed to determine if chloramines are present. The difference between total chlorine and free chlorine is combined chlorine, which shall be considered chloramines. The utility of any test is dependent upon the sensitivity and detection limits of the analytical method used. Tests for total chlorine in product water shall have a sensitivity of at least 0,1 mg/l. Alternative tests (e.g. titrometry) should be used to follow up questionable results. Tests are not required for organic or radioactive materials.

Compliance with the configuration requirements of 4.2.8 can be determined by inspection.

5.2.9 Chemical injection systems

Compliance with the requirements of 4.2.9 can be determined by inspection.

5.2.10 Reverse osmosis

Compliance with the performance requirement of 4.2.10 can be determined by the tests of 5.1.2 and 5.1.3.

If applicable, compliance with the audible alarm requirements of 4.2.10 shall be determined by use of an audiometer. Sound level measurements shall be made at a point 3 m from the audible alarm. The standard "A" scale frequency response characteristics shall be used. Alarms capable of being silenced shall be made to alarm and then be silenced. A stopwatch shall be used to verify that the alarm sounds again after an interval of no more than 180 s.

Conductivity, resistivity or TDS measurements of product water of reverse osmosis devices can be accomplished by using conventional monitors that incorporate temperature compensation features. Compliance with this requirement and the other configuration requirements of 4.2.10 can be determined by inspection.

5.2.11 Deionization

Resistivity measurements for product water of deionizers can be accomplished using conventional resistivity cells that incorporate temperature compensation features. The presence of required safety systems can be verified by inspection.

Compliance with the audible alarm requirements of 4.2.11 shall be determined by use of an audiometer. Sound level measurements shall be made at a point 3 m from the audible alarm. The standard "A" scale frequency response characteristics shall be used. Alarms capable of being silenced shall be made to alarm and then be silenced. A stopwatch shall be used to verify that the alarm sounds again after an interval of no more than 180 s.

5.2.12 Endotoxin-retentive filters

Compliance with the requirements of 4.2.12 can be shown using the test methodologies for determining bacteria and endotoxin given in 5.1.2.

5.2.13 Storage and distribution of dialysis water

5.2.13.1 Piping systems

The absence of copper, lead and zinc and the configuration of a water treatment device or system can be determined by visual inspection. Non-contribution of bacteria and specific chemical contaminants to the water by the distribution system can be verified by using the tests described in 5.1.2 and 5.1.3.

5.2.13.2 Storage tanks

Compliance with the requirements of 4.2.13.2 can be determined by visual inspection.

5.2.13.3 Ultraviolet irradiators

Compliance with the requirements of 4.2.13.3 can be determined by visual inspection.

5.2.13.4 Hot water sanitation systems

Compliance with the requirements of 4.2.13.4 can be determined by measuring water temperatures in the fluid pathway being disinfected at the most distal point for the disinfection time specified by the manufacturer.

Compliance with the configuration requirements of 4.2.13.4 can be determined by inspection.

5.2.13.5 Ozone sanitation systems

Compliance with the requirements of 4.2.13.5 can be determined by using an online monitor for dissolved ozone or by analysis of water samples using test kits based on indigo trisulfonate or DPD chemistry.

Compliance with the configuration requirements of 4.2.13.5 can be determined by inspection.

6 Labelling

6.1 General

The term “labelling,” as used in this International Standard, includes any written material accompanying any water treatment device or system, such as instructions for use and operator's manuals, or any instructions or control feature markings attached to the device or system.

6.2 Device markings

The following information shall accompany each water treatment device or system. Items a) to c) shall be directly affixed to the device or system or, in the case of disposable elements, to the immediate packaging, whereas items d) to f) may be provided in accompanying product literature.

a) Name and address of manufacturer.

b) Trade name and type of device.

c) Model and serial number.

d) A warning that product literature should be read before use (if appropriate).

e) Prominent warnings about substances (e.g. germicides) needing to be removed from the device before using the product water for dialysis.

f) Identification of fitting type or specification when necessary to prevent improper connections.

6.3 Product literature

The manufacturer shall provide literature to each user, which contains, but is not necessarily limited to, the following information.

a) Warnings that selection of water treatment equipment for dialysis is the responsibility of the user and that product water should be tested periodically.

b) A description of the device or system, including a list of monitors, alarms and ancillary devices provided as standard equipment.

c) A schematic diagram of the device or system showing the location of any valves, online monitors or sampling ports.

d) Operating specifications, such as maximum and minimum input water temperature, pressure and flow rate, limits on input water quality, pressure of product water at various flow rates, and maximum output of product water.

e) Detailed instructions for use, including initial start-up, testing and calibration, operation and meaning of alarms, operational adjustments to monitors, alarms and controls, and connections to other equipment.

f) For systems, the minimum quality of feed water required for the system to produce dialysis water meeting the chemical requirements of this International Standard.

g) For systems, a warning that although a water treatment system produces water of sufficient quality to meet the requirements of this International Standard, distribution of that water could degrade its quality to the point where it no longer meets the requirements of the International Standard if the distribution system is not maintained appropriately.

h) Safety features and warnings concerning the consequences if these features are circumvented.

i) Information pertaining to online monitors of water quality, including operational factors that could affect monitor performance (e.g. temperature).

j) In the case of systems whose product water is proportionally related to feed water quality, warnings that feed water quality shall be monitored. Since changes in product water could exceed acceptable limits if feed water deteriorates significantly, the user is responsible for monitoring.

k) In the case of activated carbon adsorption beds, a warning that exhausted or contaminated carbon should be discarded and replaced with new beds.

l) For devices regenerated or reconstituted offsite, instructions on how to safely reconnect the device to the water treatment system and how to remove any contaminant or disinfectant in the device before use.

m) A statement on regenerated or reconstituted devices, such as deionizers, certifying that there was no intermixing of regenerated or reconstituted devices returned from medical or potable water users and devices returned from process or non-potable water users. A statement that a description of the methods used to ensure that no intermixing occurred is available on request.

n) For automatically regenerated water treatment devices, identification of the mechanism (for example, lock-out valves) that prevents excessive levels of contaminants entering the product water during regeneration.

o) In the case of deionizers, a warning that deionizers should be preceded by an activated carbon adsorption bed and a recommendation that they be followed by an endotoxin-retentive filter or other bacteria- and endotoxin-reducing device.

p) In the case of ultraviolet (UV) irradiators, a requirement that the manufacturer disclose the effectiveness of the device in killing specific bacteria under specified operating conditions, and a recommendation that UV irradiators be followed by an endotoxin-retentive filter or other bacteria- and endotoxin-reducing device.

q) In the case of hot water disinfection systems, a requirement that the manufacturer disclose the effectiveness of the system in killing specific bacteria under specified operating conditions.

r) In the case of ozone disinfection systems, a requirement that the manufacturer disclose the effectiveness of the system in killing specific bacteria under specified operating conditions and that he provide a warning that product water shall not be used until the minimum time required for ozone to dissipate has elapsed.

s) In the case of hot water disinfection systems, a warning that appropriate heat-resistant materials be used for the fluid pathways to be disinfected with hot water.

t) In the case of ozone disinfection systems, a warning that appropriate ozone-resistant materials be used for the fluid pathways to be disinfected with ozone.

u) Construction materials, identified generically, that contact water.

v) Typical life expectancy, capacity or indication of the end of life of devices that are non-durable or require periodic regeneration or reconstitution, and a statement that additional information on device life expectancy or capacity relative to the user's typical feed water is available upon request. In the case of carbon adsorption beds, manufacturers or suppliers should provide a warning that unexpected exhaustion could occur because of variable feed water characteristics, including increasing pH, the presence of

species that may compete for adsorption or reaction sites on the carbon media, or materials that are deposited on the surface of the carbon media, thereby preventing chlorine and chloramines from reaching adsorption or reaction sites on the carbon granules. The only safeguard against such unforeseeable eventualities is diligent monitoring of carbon filter effluent by the user.

w) Specified water supply or operating conditions that could cause the device to fail.

x) Information about germicides and cleaning agents known to be compatible with materials used in the device, as well as information about chemicals with which materials used in the device are incompatible.

y) If applicable, a method of cleaning and disinfecting the equipment, and of removing residual germicide, so that the system of which the equipment is part is capable of meeting the requirements for microbial and endotoxin contamination given in 4.1.2.

z) Other maintenance and service instructions, including recommended preventive maintenance procedures and schedules, recommended monitoring schedules, troubleshooting guidelines intended for the user, service information, a recommended spare parts list, and a warning of the consequences if maintenance instructions are not followed.

aa) A warning that if, after installation and subsequent use, any device in the water treatment system is changed or replaced, the user should conduct appropriate tests to ensure that the revised system meets the initial design criteria.

bb) Information on storage, if allowed, of devices while not in use, including appropriate packing chemicals, storage conditions and duration.

Annex A
(informative)

Rationale for the development and provisions of this International Standard

A.1 Scope

The items included within the scope of this International Standard are equipment used to treat water for the preparation of concentrates and dialysis fluid, or for the reprocessing of dialysers for multiple uses, and the devices used to store and distribute this water.

This International Standard seeks to prevent the use of options that are hazardous to patients treated with haemodialysis and related therapies. For example, this International Standard is needed to prevent poisoning caused by formulation of dialysis fluid with water that contains high levels of certain contaminants.

Water treatment and distribution systems incorporate a variety of devices. These devices may be provided and installed by different vendors, making it difficult to assign responsibility for compliance with this International Standard to any one individual or company. To address this concern, primary responsibility for compliance with this International Standard was placed on the individual or company that specifies the water treatment and distribution system installed in a given situation. Responsibility could also lie with the vendor who assembles and installs the system, and with the manufacturer of any individual device of the water treatment and distribution system if that manufacturer specifies that their device is intended for haemodialysis applications.

A.2 Requirements

A.2.1 Dialysis water quality requirements

A.2.1.1 General

Individual water treatment devices might not provide water that meets the requirements of this International Standard in its entirety. ISO 13959 for dialysis water gives the requirement that a water system be maintained in a condition to continually meet ISO 13959-defined water quality without giving a method of accomplishing the requirements. This International Standard is directed at the manufacturer of the dialysis water treatment systems and defines the requirements that the manufacturer should meet prior to the user assuming responsibility for the water system. However, manufacturers of individual water treatment devices should be aware of the requirements for the final dialysis water and that they should be prepared to recommend other water treatment devices that may need to be used in conjunction with their device to produce water which meets the requirements of this International Standard.

A.2.1.2 Microbiology of dialysis water

The supplier of water treatment equipment is responsible for recommending a method of cleaning the equipment so that dialysis water meeting the microbial requirements of ISO 13959 can routinely be produced when typical feed water is presented. Beyond this qualification, it becomes the responsibility of the user of the system to monitor the system for ongoing compliance with ISO 11663. The rationale for these microbiological contaminant requirements is set forth in Annex A of ISO 13959:2009.

A.2.1.3 Maximum level of chemical contaminants

The rationale for the chemical contaminant requirements is set forth in Annex A of ISO 13959:2009.

Tables B.1 and B.2 should not be taken as a definitive list of harmful substances, but as a partial listing of those that might reasonably be expected to be present and have clinical implications. Iron is not included because it does not enter the patient's blood in sufficient quantities to cause toxicity. Iron can, however, cause fouling of water treatment devices (see 4.2.1.1) or dialysis fluid supply systems. While a specific limit was not set, water treatment equipment suppliers are encouraged to consider the iron content of the feed water when recommending suitable equipment. A concern was raised regarding the injection of formulated phosphates (known as polyphosphates) primarily to bind iron and manganese to avoid the staining of fixtures and clothing. The concern was raised that this practice could cause significant problems in water treatment. Some municipal water suppliers were considering the use of chlorine dioxide as a disinfectant for potable water supplies. Chlorine dioxide breaks down in water to yield chlorite, chlorate and chloride ions. Little information about the potential for chlorine dioxide and its daughter products to be toxic to haemodialysis patients could be found. A limited study of 17 patients unknowingly treated with water prepared by carbon adsorption and reverse osmosis from water disinfected with chlorine dioxide showed no evidence of adverse effects (Ames and Stratton[2]). In that study, the water used to prepare dialysis fluid contained 0,02 mg/l to 0,08 mg/l of chlorite ions and no detectable chlorate ions. However, the patient population was small, and potentially important haematological parameters were not measured. Further, there were only sparse data included on the removal of chlorine dioxide, chlorite ions and chlorate ions by carbon adsorption and reverse osmosis, and it was not clear that sufficiently sensitive methods were available for their analysis in a dialysis facility. Therefore, there was no basis for setting maximum allowable levels of chlorine dioxide, chlorite ions or chlorate ions in water to be used for dialysis applications, or for making recommendations on methods for their removal at that time. However, in specifying water treatment systems, manufacturers of such systems should be aware of the possibility that municipal water suppliers may add chlorine dioxide to the water.

A.2.2 Water treatment equipment requirements

A.2.2.1 General

A.2.2.1.1 Water treatment system

The supplier of the complete water treatment system is responsible for assuring that the water produced by the system can routinely meet the maximum allowable chemical contaminant levels specified in Tables B.1 and B.2, or the prescription of the physician, at installation. Beyond this qualification, it becomes the responsibility of the physician in charge of dialysis to monitor the system to assure that the treatment device or devices maintain an acceptable level of purity of the water. Variations in water quality or the presence of as-yet-unidentified toxic substances will obviously compromise the system's safety (Keshaviah *et al.*[13]). Such variations typically do occur, and while the supplier cannot be held accountable for the performance of the water treatment system during such variations, selection of water purification equipment should include careful consideration of methods to cope with such changes, many of which can be anticipated through consultation with state and local water authorities.

The medical director has the ultimate responsibility for the selection and use of water treatment devices on the basis of the supplier's recommendations. If a supplier is convinced that the local water quality is such that the selection of a minimum system does not provide an adequate margin of safety, then the supplier should recommend additions to the system or alternative systems with corresponding rationale. Continued monitoring of the water supply is necessary to maintain treatment methods consistent with safety.

A.2.2.1.2 Materials compatibility

Non-toxicity of construction materials for haemodialysis water treatment equipment is of major importance. Some well-recognised non-toxic materials include certain stainless steel formulations, silicon rubber, borosilicate glass, polypropylene, polyvinylchloride (PVC), chlorinated PVC (CPVC), polyvinylidene fluoride (PVDF), polyethylene, cross-linked polyethylene (PEX) and polytetrafluorethylene (PTFE). Data are now available that demonstrate that materials once regarded as inert can in fact be toxic in this application (e.g. copper leaches from copper conduits, especially in the presence of low pH, which can result when a deionizer

is exhausted) (Keshaviah *et al.*[13]). Other materials have been documented as being hazardous to the patient (e.g. brass, zinc, iron and aluminium), and these materials should also be avoided. The hidden hazard with respect to construction materials derives from long-term cumulative toxicity. Patients on haemodialysis might well have a life expectancy in excess of 10 y, and this fact should be acknowledged when selecting construction materials. Direct testing for chemicals leached from devices cannot be specified at this time because of a lack of suitable procedures.

Repeated exposure to ozone or hot water might have a deleterious effect on some plastic or metal materials. Therefore, manufacturers are required to include warnings that only ozone- or heat-compatible materials be used in piping systems intended for use with ozone or hot water disinfection devices, respectively (see 6.3).

A.2.2.1.3 Regenerated or reconstituted devices

Regenerated or reconstituted devices are subject to bacterial contamination that can cause excessive bacterial counts in product water (see 4.1.2). Disinfection procedures are required to minimize this risk. When devices are regenerated at a central facility, there is a risk of cross-contamination and improper disinfection and rinsing (Keshaviah *et al.*[13]). Some exchange-type deionizers are used for both dialysis and industrial recovery of plating metals, such as chromium and silver, from effluent process water. In some regeneration facilities, resins from both process or non-potable users and from medical or potable users are regenerated together as a batch. Traces of these toxic metals will remain bound to the resins and could be eluted into water during subsequent use. For that reason, such mixed use is prohibited in this International Standard.

A.2.2.1.4 Disinfection protection

Disinfection procedures can render product water unsafe because of toxic chemicals or excessive temperatures. Therefore, provision was made for restoring the water treatment system to a safe condition after disinfection. Although the user is responsible for carrying out manual disinfection procedures, the manufacturer should demonstrate that recommended disinfection procedures meet the requirements of 4.2.1.4.

A.2.2.2 Backflow prevention device

A backflow prevention device isolates the water treatment system from the potable water supply, thereby protecting the potable water system from possible contamination in the event of a sudden reduction in pressure in the potable water supply.

A.2.2.3 Tempering valves

The performance of many water treatment devices is temperature sensitive. In less temperate climates, seasonal fluctuations in cold water temperature could impact the performance of these devices. A tempering valve can be used to blend hot and cold water to provide a constant feed water temperature independent of any seasonal changes in feed water temperature. Excessive water temperatures resulting from malfunction of a tempering valve can damage downstream devices, including reverse osmosis membranes and plastic pipes and pipe fittings. For that reason, consideration was given to requiring that tempering valves be fitted with a water temperature monitor that activates an audible alarm in the event that a high temperature is sensed. While recognising the potential for equipment to be damaged by hot water, no consensus could be reached on the need for such a requirement.

A.2.2.4 Sediment filters

Accumulation of organics, bacteria, and algae in filters can lead to proliferation of bacteria to the point of overloading downstream devices or producing dangerous endotoxin levels. Use of opaque housings to reduce the light that promotes algae growth and differential pressure monitoring can reduce this risk.

A.2.2.5 Cartridge filters

Accumulation of organics, bacteria and algae in filters can lead to proliferation of bacteria to the point of overloading downstream elements or producing dangerous endotoxin levels. Use of opaque housings to reduce the light that promotes algae growth and differential pressure monitoring can reduce this risk. In the pretreatment cascade, transparent filter housings can be useful because they allow any carbon or resin leakage to be seen without the need to break the integrity of the system. The housing can be cleaned to remove any growth when the filter cartridges are changed. For this reason, use of opaque housings for cartridge filters is recommended, but not required. If transparent housings are used, they should not be exposed to natural light, in order to minimize proliferation of algae.

A.2.2.6 Softeners

The process by which "hard" water (containing high levels of calcium and magnesium) is made "soft", involves the exchange of sodium ions for the calcium and magnesium in the water supply. The resin should be regenerated with brine to sustain capacity for exchange. Regeneration can be either manual or automatic with a timer to regenerate outside operating hours. During regeneration, excess sodium can enter the product water stream if there is a temporary interruption of power, a malfunction in regeneration control or inadequate water pressure. There are no monitors on a softener to detect excess sodium in the product water stream, and the physiological effects of excess sodium in the patient are severe (Nickey *et al.*[18]; Robson [21]). Therefore, protection against such excessive levels of sodium, as can occur during regeneration of a water softener, is required. An automatic bypass valve most easily provides this protection during the regeneration cycle.

A.2.2.7 Anion exchange resin tank

High levels of organic matter in the source water can foul carbon adsorption media. Organic molecules (usually very large) are attracted to carbon and become attached at the pore sites, effectively blocking the pore and sealing off the surface area within that pore. As organic molecules accumulate on the surface of the carbon, there is less surface area available for removal of chlorine. Organic scavengers operate similar to a water softener, exchanging anions and organic matter for chloride ions. Source water testing for organics (TOC or tannins) can indicate if an organic scavenger will help protect carbon adsorption media.

A.2.2.8 Carbon adsorption media

Carbon adsorption beds are particularly prone to bacterial growth because of their porosity and affinity for organics. More stringent requirements for the installation of carbon adsorption beds and their monitoring are included because of continued reports of clusters of haemolysis related to insufficient removal of chloramines from municipal water supplies (Caterson *et al.*[8]; Tipple *et al* [23].; Ward [27]). In the United States, changes to the *Safe Drinking Water Act*, designed to eliminate lead and copper from tap water (Petersen and Thomas [20]), have reinforced the need for careful monitoring of carbon adsorption beds, since the increase in water pH that can accompany the institution of these changes may decrease the adsorptive capacity of carbon for chloramines.

Activated carbon may be regenerated by a number of techniques, including oxidation at high temperatures and stripping with low-pressure steam or solvents. Regeneration of activated carbon, also known as reactivation, is used in industrial applications where activated carbon can be used to remove organic and inorganic substances such as pollutants from process streams. No evidence that regenerated carbon was being used for haemodialysis applications could be found. However, it was deemed prudent to prohibit the use of regenerated carbon in haemodialysis applications to avoid any potential hazard resulting from residual toxins that could remain in the carbon following regeneration.

Depending on the source material used for its manufacture, and the manufacturing process, granular activated carbon can contain carbon fines and other contaminants, such as aluminium. If present, these substances will leach out of a carbon adsorption bed during the initial stages of operation. Carbon fines can contribute to fouling of reverse osmosis membranes downstream of the carbon adsorption beds and any metal ions can add to the burden of contaminants, which should be removed from the water. Acid washing of carbon minimizes the amount of fines and other contaminants, and a requirement for the use of acid-washed carbon was considered. No consensus could be reached on this issue, because rinsing of carbon adsorption beds before they are placed online in a water treatment cascade will also effectively remove fines and other contaminants.

The requirement for two adsorption beds in series and a 10 min empty-bed-contact-time was waived for portable dialysis systems because of the impracticality of providing these features while retaining the portability of the system. However, when a single adsorption bed is used, it is important to ensure that the bed has adequate capacity to remove chloramines for the duration of an entire treatment given the typical feed water concentration of chloramines in the setting where the bed is being used.

Although treatment of water by carbon adsorption is the usual method of meeting the requirement of 4.1.3 when the feed water contains chloramines, in certain situations, such as acute or home dialysis with portable water treatment systems, it might not be practical to use the volume of carbon required for this purpose. In such circumstances, combining limited carbon adsorption with the addition of ascorbic acid to the acid concentrate has been used to eliminate chloramines from the final dialysis fluid (Ward [27]). It should be noted that some minimum contact time is required for ascorbic acid to neutralize chloramines in water. If ascorbic acid is being used to neutralize chloramines, and unexplained red blood cell destruction or anaemia occurs, the effectiveness of the ascorbic acid neutralization of chloramines should be investigated.

In most circumstances, conventional carbon adsorption systems provide months of effective chlorine/chloramine removal. Occasionally, conventional carbon adsorption systems experience premature breakthrough necessitating carbon bed replacement/exchange within days rather than months. These occasions could be episodic or persistent in nature. Episodic carbon filter breakthrough is often associated with periodic municipal water treatment practices, such as short-term substitution of free chlorine for chloramine. Persistent difficulties with premature breakthrough of carbon adsorption systems could be related to the source water itself (pH, TOC level, etc.) or a routine municipal water treatment practice, such as the addition of corrosion inhibitors. The occurrence of these problems seemed to be increasing. Therefore, clauses on optional water purification system devices that might help address recurrent premature exhaustion of carbon adsorption media or enhance the efficiency of the carbon media were added. Two approaches were included: anion exchange resins that scavenge large organic molecules that can coat the carbon surface, and systems that inject sodium bisulfite, which reduces chloramine to chlorine, or acid to adjust the pH to the optimal range for removal of chloramine by carbon. Including the use of redox alloy media (RAM), also referred to as kinetic degradation fluxion (KDF), was also considered. This material can be an effective pretreatment for conventional carbon filters experiencing premature breakthrough due to municipal short-term substitution of free chlorine for chloramine or for supply waters having high organic loading. A disadvantage of KDF media is that both copper and zinc are eluted from the medium, albeit at very low levels. Concerns about how the eluted copper and zinc might affect downstream devices, together with questions about the effectiveness of KDF media, lead to the omission of this alternative.

A.2.2.9 Chemical injection systems

There were reservations about the addition of chemicals to the water. However, it was recognized that the addition of chemicals could be necessary in some circumstances if a facility is to meet the maximum contaminant levels set forth in 4.1.3. For example, if the municipal water contains high levels of *N*-chloramines or chloramine in the presence of orthophosphate or polyphosphate, injection of sodium bisulfite could be one of the few options available for chloramine removal. If chemical injection is used in the pretreatment cascade, users should ensure that the addition of the chemical does not interfere with the operation of subsequent purification processes, including the primary purification process. For example, the performance of thin-film composite reverse osmosis membranes can be affected by the pH of the feed water. At pH levels below 7, the rejection of fluoride can be substantially reduced, compared to its rejection at a pH of 8.

A.2.2.10 Reverse osmosis

A reverse osmosis system should demonstrate delivery of water meeting the requirements of 4.1.2 and 4.1.3; otherwise, additional treatment devices should be recommended to the user. Monitoring requirements for reverse osmosis systems are recommended on the basis of totally different degradation characteristics of these systems as compared with deionizer systems. On initial setup, the reverse osmosis device should have a rejection rate that ensures that the product water of the water treatment system meets the requirements of 4.1.3. Because this rejection rate varies with different installations, an absolute level is not required. Monitoring is defined in terms of the salt passage rate, or percent rejection and a threshold level of product water resistivity or conductivity. Compliance with both monitored parameters is required, since an increase in feed water contaminants could result in product water unsuitable for haemodialysis applications even though the percent rejection of the membrane modules remains high.

Consensus could not be reached on how to establish the alarm limits for rejection and product water resistivity or conductivity. As noted above, changes in feed water quality will result in changes in product water quality even though rejection remains constant. Also, a significant change in the feed water concentration of one trace inorganic contaminant might not appreciably alter the product water resistivity even though the product water concentration of that contaminant exceeds the allowable limit. For that reason, some felt that routine analysis of feed water quality should be emphasized. Others felt that the rejection alarm limit could be set based on the reduction ratio for each contaminant that can be achieved by reverse osmosis (Luehmann *et al.*[15]) and the assumption that the feed water would meet the requirements of the *Safe Drinking Water Act* or other applicable standards. Either approach could be effective when incorporated into an overall monitoring programme designed to protect the patient against exposure to contaminant levels in excess of those listed in Tables B.1 and B.2.

Consensus could not be reached regarding the inclusion of a requirement that reverse osmosis systems incorporate a means of diverting the product water to drain in the event of a product water conductivity or rejection rate alarm. Some felt that a divert-to-drain should be required because reverse osmosis is frequently the primary means of water purification. However, others felt that including a divert-to-drain should be optional. They pointed out that, because reverse osmosis membranes tend to fail gradually, the risk is different from exhaustion of a deionizer where very high levels of contaminants, such as fluoride, can occur abruptly in the product water because of competitive binding at the ion exchange sites of the deionizer resin. Furthermore, with direct feed water distribution systems, a divert-to-drain would cause an immediate alarm condition with all dialysis machines as a result of interrupting their water supply. Under such circumstances, the ability to discontinue dialysis effectively could pose the lowest risk to the patients. Therefore, a divert-to-drain was included as a recommendation and not as a requirement.

The question of whether or not audible alarms should be capable of being silenced provoked some discussion. On one hand, some felt that audible alarms should not be capable of being silenced because the alarm condition could be overlooked, allowing a dangerous situation to ensue. On the other hand, an audible alarm capable of being temporarily silenced was suggested so that the operator would have a relatively unharried period of time to correct the fault condition. It was concluded that the ability to silence an audible alarm for up to 180 s was a reasonable requirement.

A.2.2.11 Deionization

Deionizer systems, during exhaustion, have the capability of releasing into the water potentially harmful contaminants at levels much higher than are present in the untreated feed water (Johnson and Taves [12]; Bland *et al.*[6]). The monitor level of 1 MΩ·cm specific resistivity was selected as the point at which most of the useful capacity of the deionizers used in dialysis water treatment has been consumed and below which rapid degradation of ion removal efficiency takes place; 1 MΩ·cm specific resistivity is not the minimum safe value for dialysis water, but deionizer systems producing water dropping below this value are in danger, during the following dialysis treatment, of producing water high in toxic contaminants as the final deterioration of resin accelerates. A requirement that the product water be diverted to drain was included because of the acute danger that an exhausted deionizer can pose to patients (Arnow *et al.*[4]). The requirement for activated carbon adsorption in advance of the deionizer prevents generation of possibly carcinogenic nitrosamines (Simenhoff *et al.*[22]). Deionizers are subject to bacterial contamination because of the porous structure of the resins. Although the level of bacterial contamination in product water from deionizers varies widely, it is generally highest after the deionizer has been idle for some time and lowest after continuous use. Because deionizers are usually placed last in a purification cascade, they should be followed by an endotoxin-retentive filter or another bacteria and endotoxin removing device to prevent bacterial contamination of the water storage and distribution system.

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A.2.2.12 Endotoxin-retentive filters

Endotoxin-retentive filters are increasingly being used to provide water of high microbiologic quality for dialysis applications. Endotoxin-retentive filters include ultrafilters that remove endotoxin primarily by size exclusion, although some can also remove some endotoxin by adsorption to the membrane material, and microfilters that remove endotoxin primarily by adsorption to the membrane material. Because of the two different mechanisms of endotoxin removal, and because the role of endotoxin-retentive filters is to remove bacteria and endotoxins, they have been defined in these terms. This choice also provides a basis for monitoring the performance of endotoxin-retentive filters after they have been installed in a water treatment purification system. Consensus could not be reached regarding minimum performance criteria for the removal of bacteria and endotoxins by an endotoxin-retentive filter. One factor contributing to this impasse is the dependence of filter performance on the test conditions. Therefore, it was decided to require that manufacturers disclose the minimum performance of their device and that the device be required to perform to at least this level under stated operating conditions. Some considered that an endotoxin-retentive filter should be able to reduce the concentration of bacteria in the feed water to the filter by a factor of at least 10^7 and that of endotoxin by a factor of at least 10^3. Methods for determining bacteria and endotoxin rejection by ultrafilters have been published by the Japanese Standards Institute [10], [11] and ASTM [5].

The recommendation to use endotoxin-retentive filters in a cross-flow configuration is aimed at preventing excessive replacement of membrane modules, which could result from rapid fouling if the filter is operated in the dead-end mode. However, a dead-end configuration might perform satisfactorily in situations where the water quality is generally good (for example, as final filtration of water immediately before its use in dialyser reprocessing equipment). Differential pressure measurements can be used to monitor fouling of both cross-flow and dead-end filters.

A.2.2.13 Storage and distribution

A.2.2.13.1 Piping systems

The distribution system has been implicated in several bacterial contamination episodes involving dialysis patients (Petersen *et al.*[19]). Specific design criteria, such as minimum flow velocities, to minimize bacterial proliferation and biofilm formation (Chapman *et al.*[9]) were considered. Desirable design criteria include use of a distribution loop, an absence of multiple branching and dead-ended pipes, the use of simple wall outlets with the shortest possible fluid path, a minimum of pipe fittings, and the use of valves with minimal dead space. Also, joints between sections of piping and between piping and fittings should be formed in a manner that minimizes the formation of crevices and other voids that could serve as sites for bacterial colonization. Agreement could not be reached concerning a minimum flow velocity. Some were of the opinion that the low shear stresses existing at the internal surface of a pipe operating at flow rates that are feasible in distribution systems for dialysis water are insufficient to prevent bacterial adhesion and biofilm formation. On the other hand, data from the semiconductor industry were presented showing that a Reynolds number of 3 000 in a piping system was sufficient to prevent bacterial contamination in water (Libman [14]). A Reynolds number of approximately Re 3 000 is obtained with a flow velocity of about 0,15 m/s in a 2 cm diameter pipe (0,5 ft/s in a 3/4" diameter pipe). However, even in systems operating with Re 3 000, biofilm was found on the internal surface of the pipes (Libman [14]). Further, in many dialysis facilities there is no flow through the distribution system when the dialysis facility is not in operation, such as at night and on Sundays. Even if it were possible to specify a minimum flow velocity that was effective in reducing biofilm formation and bacterial contamination, use of such a minimum flow velocity would not provide a substitute for regular disinfection of the distribution system.

Direct feed systems commonly return water from the dialysis water distribution loop to the feed side of the reverse osmosis unit, before the pressurizing pump. With this configuration, it is possible for water from the feed side of the reverse osmosis unit to flow retrograde into the dialysis water distribution loop if the pressure in the distribution loop suddenly decreases as the result of a sudden increase in demand for dialysis water. Since retrograde flow allows contaminated water to enter the dialysis water distribution system, it was considered necessary to recommend some means of preventing retrograde flow. A common method is to include dual check valves at the end of the distribution loop. Some were concerned that there is no means of monitoring the integrity of these valves. A second approach is to return the dialysis water into a break tank at the inlet to the pressurizing pump of the reverse osmosis unit.